

## **REMARKS**

### ***Claim Amendments***

Claims 1, 5-8, 13, 15, 16, 29-30, 32, 35-38 and 43-44 are amended. Claims 18-21, 48 and 51-52 are canceled. Claims 53-56 are newly added.

Support for the amendments to claims 1, 13 and 32 can be found throughout the specification and in the claims as originally filed. *See, e.g.*, page 21, lines 4-8. Support for the amendments to claims 7 and 37 may be found throughout the specification and in the claims as originally filed. *See, e.g.*, page 13, lines 16-19. Support for the amendments to claims 15 and 16 may be found throughout the specification and in the claims as originally filed. *See, e.g.*, original claims 13, 15 and 16. Support for claims 53, 55 and 56 may be found throughout the specification and in the claims as originally filed. *See, e.g.*, page 14, lines 14-16. Support for claims 54 may be found throughout the specification and in the claims as originally filed. *See, e.g.*, page 11, lines 25-28. Support for Claims 5-8, 29-30, 35-38 and 43-44 may be found throughout the specification and in the claims as originally filed. Applicants respectfully request entry of the above amendment and submit that the above amendment does not constitute new matter.

Upon entry of the foregoing amendments, claims 1, 3, 5-17, 29-32, 34-47, 49, 50 and 53-56 will be pending in the application.

### ***Withdrawn Rejections***

Applicants appreciate the Office Action's withdrawal of all previous rejections.

#### ***Statement of Substance of Interview Under 37 C.F.R. § 1.133(b)***

In accordance with 37 C.F.R. § 1.133(b) and M.P.E.P. § 713.04, Applicants provide a summary of the interview among Examiners Guzo and Joike, Applicants and Applicants' representatives on June 5, 2008. Applicants and Applicants' representatives greatly appreciate the courtesies extended by the Examiners.

During the interview, Applicants' representatives explained that the methods disclosed in U.S. Patent No. 6,056,954 ("the '954 patent") and the claimed methods are fundamentally distinct. Applicants' representatives also pointed out that the '954 teaches away from the claimed invention. The Examiners indicated that the outstanding rejections

would be withdrawn if these arguments are presented in response to the Office Action. *See* Examiner's Interview Summary.

***Claim Rejections — 35 U.S.C. § 103(a)***

Claims 1, 5, 7-9, 32, 35, 37-39 and 48-50 stand rejected as allegedly being unpatentable over the '954 patent in view of U.S. Pub. No. 2005/0260171 ("the '171 publication").

Applicants respectfully disagree and traverse this rejection.

**A. The '954 Patent and the Claimed Invention Are Directed to Fundamentally Distinct Methods**

The claims relate to various methods which include a step of providing an individual with a composition containing bacteriophage.

The '954 patent does not teach such methods. Rather, as the Office Action acknowledges, the '954 patent is directed to methods of using lytic *enzymes*. *See* Office Action, page 5 ("...the reference is teaching the use of lytic enzymes instead of bacteriophages."). Nonetheless, the Office Action asserts that because bacteriophages will cause production of lytic enzymes, "it would have been obvious to one of skill in the art to use the entire bacteriophage, instead of the lytic enzymes..." *Id.*

Applicants respectfully disagree.

Bacteriophages and lytic enzymes kill bacteria in a significantly different manner. Bacteriophages adsorb to bacterial cell walls and inject their DNA into the bacteria's cytoplasm.<sup>1</sup> Within minutes of penetrating the bacterial cell wall, the bacteriophage stops the bacterium's expression system and thus kill the bacterium. The bacteriophage then uses the bacterium's metabolic machinery and replicates its genome. At the end of bacteriophage life cycle, lytic enzymes are produced, the previously-killed bacterial cell bursts and phage progeny are released. Therefore, when a bacteriophage infects a bacterium, the bacterium is dead prior to lysis. On the other hand, lytic enzymes kill bacteria by degrading the cell wall and lysing the bacteria.

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<sup>1</sup> *See, e.g.,* Mathews, C. K. (1994). An overview of the T4 developmental program. *Molecular Biology of Bacteriophage T4*. K. J. D. Washington, D.C., American Society for Microbiology: 1-8 (discussing the life cycle of a bacteriophage). This article was submitted in Applicants' previous response.

Applicants also note that in the method of the '954 patent, there must be enough of the lytic enzyme to kill all of the bacteria when the enzyme is initially administered. This contrasts with bacteriophage. Indeed, since bacteriophage replicate in the bacterial cell and bacteriophage progeny are subsequently released, it is not necessary to apply enough bacteriophage to kill all of the bacteria when the bacteriophage is initially administered. Accordingly, the administration and modes of action of bacteriophages and lytic enzymes differ significantly.

**B. The '954 Patent Teaches Away from Using Bacteriophages**

The '954 states that there are "drawbacks" from the direct introduction bacteriophages. *See* '954 patent, col. 1, lines 63-65. Specifically, the '954 patent states that there "must be the right number of phages to attach to the bacteria," otherwise, there will be "no production of the lysing enzyme," i.e., the bacteria would not be lysed and killed. '954 patent, col. 2, lines 1-4. Contrary to the Office Action's assertions, one of ordinary skill in the art, in view of the '954 patent, would have been dissuaded from using bacteriophages to produce a lytic enzyme. Accordingly, the '954 patent teaches away from using bacteriophages.

**C. The '171 Publication Fails to Remedy the Deficiencies of the '954 Patent**

The Office Action acknowledges that the '954 patent does not teach reducing the level of colonization of the bacteria by at least one log. Office Action, page 5. To remedy this deficiency, the Office Action cites to the '171 publication. In particular, the Office Action asserts that the '171 publication teaches a reduction in colonization by at least one log. *Id.* (citing to Example 9).

Applicants respectfully disagree and submit that the '171 publication does not teach or mention any reduction in colonization whatsoever. Rather, the '171 publication relates to treating bacterial infections. *See, e.g.*, Abstract, ¶¶ [0002], [0011]. In particular, Example 9 teaches a method of measuring bacterial levels *in vitro* and does not actually treat an infected individual. The distinction between colonization and infection was previously discussed by Applicants. *See* Response filed April 16, 2007, pages 15-16. Accordingly, the '171 publication does not remedy the deficiencies of the '954 patent.

#### **D. The Claims Recite Non-Systemic Modes of Administration**

The claimed methods relate to the reduction of colonization to reduce the risk of infection, and not to methods of treating systemic infections. Applicants have amended the claims to recite non-systemic modes of administration, thereby highlighting this distinction.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

Claims 3, 6, 10-14, 17, 29-31, 34, 36 and 40-47 stand rejected as allegedly being unpatentable over the '954 patent, as applied to claims 1, 4, 5, 7-9, 32, 35, 37-39 and 48-50 above, and in view of Carlton et al. (*Archivum Immunologiae et Therapiae Experimentalis*, 47: 267-274, 1999, hereinafter "Carlton") and Risi et al. (*Am J. Infect. Control*, 26: 594-604, 1998, hereinafter "Risi").

The Office Action reiterates the purported teachings of the '954 patent and the '271 publication, but acknowledges that these references do not teach that "the patient is immunocompromised, the pathogenic bacteria are VRE or MDRSA or multi-drug resistant *Pseudomonas*, the composition can contain a plurality of bacteriophage strains to produce lytic infections against a plurality of bacterial species, or that the method can also be used to reduce the incidence of bacterial infections of patients admitted to a hospital." Office Action, pages 6.<sup>2</sup>

Applicants respectfully disagree and traverse this rejection.

As discussed above, the combination of '954 patent and the '171 publication does not teach a method of reducing the risk of infection or sepsis by providing a composition comprising a bacteriophage to reduce the level of colonization by at least one log.

Carlton does not remedy the deficiencies of the '954 patent and the '171 publication. Carlton generally relates to bacteriophage therapy of patients who have already developed an illness. See, e.g., Carlton, page 271, col. 2.

Risi also fails to remedy the deficiencies of the '954 patent and the '171 publication. Among other things, Risi does not teach or mention the use of bacteriophages.

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<sup>2</sup> Applicants note that the Office Action states that the '954 patent "...teach[es] a method of using lytic bacteriophages..." Office Action, page 7. This appears to be a typographical error as the Office Action also states that '954 patent "is teaching the use of lytic enzymes instead of bacteriophages." *Id.* at page 5.

Applicants submit that one of ordinary skill in the art would have no reason to combine the teachings of the '954 patent, the '171 publication, Carlton and Risi. Even if one of ordinary skill in the art had a reason to combine these teachings, which they would not, the combination would not teach each and every limitation. Accordingly, Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

**CONCLUSION**

In view of the foregoing, Applicants respectfully request an indication of allowance of all claims.

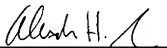
This response is being filed within the three-month time period set forth in the Office Action. Accordingly, no fees are due. Should any fees be required to enter and consider this response, or keep the application pending, the Commissioner is authorized to charge such fees to **Deposit Account No. 50-0206**.

Respectfully submitted,

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